the presence of dense CO_2 to create such spheres by then mixing it with the SLS and dextrin in the required ratios.

The invention is equally applicable to cyclosporine derivatives, such as valspodar.

Example 5

Fenofibrate is another solid substance which can be manipulated by the method of the invention. Fenofibrate (2-[4-(4-chlorobenzoyl) phenoxy]-2-methyl-propanoic acid, 1-methylethyl ester) has a molecular weight of 361 g/mol and a melting point at atmospheric pressure of 79-82°C. Using the method of the invention, fenofibrate was processed into micron sized particles.

CO_2 gas was solubilized in molten fenofibrate and then depressurised rapidly by spraying the solution through a nozzle or orifice as described above, using the apparatus illustrated in Figure 2. In this configuration, gas is forced from the bottom of the Jerguson Cell to the top. This configuration maintains the gas solution below saturation, thus reducing blockages in the 50 micron nozzle. As a result of the pressure drop, particles were precipitated as a fine powder.

Fenofibrate was processed using the following conditions:

Pre-expansion pressure: 190 bar.

Pre-expansion temperature: 50°C.

Post-expansion pressure: The pressure in the expansion chamber was maintained below 3 bar, with a pressure relief valve.

Post-expansion temperature: The temperature in the expansion chamber was room temperature.

Nozzle size: 50 micron internal diameter.

Particle Collection device: Particles are collected in a Whitey chamber. A low pressure relief valve was used to ensure that the pressure in the collection chamber remained below 3 bar. A 0.5 micron filter was placed at the outlet line of the particle collection device.

The melting point depression of fenofibrate varied as a function of temperature. At and below 35°C, no melting point depression was evident below 200 bar. At 40°C, melting occurred at 88 bar and at 50°C, melting occurred at 68 bar. Therefore at 50°C, the method of the invention is applicable at pressures greater than 68 bar.

Unprocessed fenofibrate is provided as large (60 micron) irregular crystals. SEM images at 2 different magnifications, namely 100x (Figure 11a) and 2510x (Figure 11b), of fenofibrate processed at 50°C and 190 are shown in Figure 11. The particles are not aggregated, and have a particle size of approximately 5 – 10 microns.

Example 6

Gemfibrozil (5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoic acid) is another example of a pharmaceutically active compound which may be a solid substance in the method of the invention, and subjected to dense carbon dioxide. Gemfibrozil has a molecular weight of 250 g/mol and a melting point at atmospheric pressure of 58-61°C. The method of the invention can therefore be used in processing gemfibrozil. Gemfibrozil is very poorly soluble in water and is used as an anti-lipidic drug. Gemfibrozil was used as supplied by Australian Pharmaceutical Ingredients, Sydney, Australia. The material is white in colour.

As before, gemfibrozil was packed in a glass pasteur pipette stoppered with glass wool, and placed in a Jerguson Cell. The Jerguson was thermally equilibrated. Carbon dioxide was introduced to the cell thereby increasing the pressure. The onset of a melting point depression was monitored visually. Again, gas was forced from the

bottom of the Jerguson, to the top. At 50°C, a melting point depression was observed at 40 bar.

SEM images were taken, using a Hitachi S4500 electron microscope. The samples were chromium coated for 60 seconds with a current of 125 mA, with a Emitech E4500 coater. Figure 12 contains SEM images of gemfibrozil processed by the method of the invention using CO_2 at a pressure of 190 bar and temperatures of 50°C (image (a)) and 25°C (image (b)).

The particles formed are approximately 5 microns in size. Particles formed with the dense gas at a sub-critical condition are more polydisperse than those formed at 50°C. At both conditions, around 80ml of carbon dioxide at 190 bar was used to produce particles, and in both cases around 100 mg of gemfibrozil was produced. The size of the batch was limited by the filter on the outlet of the expansion chamber blocking. The powder was a free flowing fine powder.

It will be understood that the invention disclosed and defined in this specification extends to all alternative combinations of two or more of the individual features mentioned or evident from the text or drawings. All of these different combinations constitute various alternative aspects of the invention.